PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of:

Metin COLPAN

Serial No.: 08/244,530 Group Art Unit: 1803

Filed: August 2, 1994 Examiner: L. Crane

For: DEVICE AND A PROCESS FOR THE ISOLATION OF NUCLEIC ACIDS

**RESPONSE**



Assistant Commissioner of Patents
Washington, D.C. 20231

Sir:

Applicant submits the present response to the Office advisory dated July 23, 1996.

The present claims are 40-61.

In the Advisory Action the Examiner maintains that Little contains motivation to substitute the three desalting methods used in Henco (column 7, lines 44 to 46) with the silica separation method according to Little. Applicant respectfully disagrees.

Henco **starts** with DNA having a relatively low concentration of salt, which is not comparable with the situation Little address in the introductory portion of his disclosure. The DNA fractions dealt with in the paragraph cited by the Examiner are obtained after a cesium chloride gradient centrifugation.

With respect to the samples which would be obtained in "too high a dilution," appellant submits that Henco teaches a method for separating DNA, wherein the DNA is not highly diluted in the eluate obtained from the method.

Since the DNA is first absorbed on the chromatographic matrix and is afterwards desorbed in one elution step, the concentration of DNA is considerably high in the feral

eluate. By analogy, therefore, Little's separation would be considered by the skilled person as an alternative separation method for isolating DNA; not as a mere substitute desalting step.

In contrast, the method of the presently claimed invention utilizes, for the first time, the effect of silica disclosed in Little for such desalting steps. Originally, Little was not at all dealing with a desalting method, but with a separation method starting with highly concentrated salt solutions. This is evident from column 2, line 17 et seq. of Little, were it is stated: "This invention is directed to a process for the purification of plasmid and other DNA, both single-stranded and double-stranded, by immobilizing the DNA onto diatomaceous earth particles and eluting the DNA with water or low salt buffer (emphasis added)."

Therefore, the skilled artisan would not consider the Little reference for just employing a desalting step of a sample obtained according to Henco. Applicant respectfully submits that the argument of the Examiner is a matter of hindsight; picking out features of the claimed process and trying to find the features in some piece of prior art. With all due respect, the argument for obviousness fails to consider the question: Why would the skilled person have believed that Little would be a suitable "desalting step" in a method according to Henco? Applicant emphasizes that the inventive objective of the present claimed invention was to show that Little's purification process could also be used for desalting of a DNA-containing fraction. However, Little is not concerned in any way with desalting of a sample. Little is concerned with purification of DNA found in a high-salt solution.

Henco, however, does not yield such a sample having nucleic acid in a high salt environment.

The Examiner maintains that Sternberg contains motivation to pass cells through stacked filtered membranes. However, the Sternberg reference deals with affinity membranes. This is evident from the passage cited by the Examiner, as well as for the Sternberg example appearing at column 3, line 6 et seq. However, the asymetric filters mentioned in the present claimed invention are not affinity membranes. Affinity membranes are membranes that are treated with affinity ligands. This can be derived also from column 4, lines 43 et seq. of Sternberg.

Applicant submits that it is unclear what column 10, lines 60 et seq., of Sternberg would disclose with respect to a "sticky mass" obtained by disintegration of cells according to the present invention occurs. From this example, it seems that soluble horse proteins were separated in a one-step adsorption. Therefore, the relevance of the cited passage with respect to the present invention is not apparent.

Whether or not the "digested cells" would meet those disclosed in Henco et al., the significance of this allegation is not apparent. Henco does not disclose the use of a filter having decreasing pore sizes as claimed in present claim 61.

In contrast to Examiner's opinion, column 4, lines 47-48 of Henco states that no long time centrifugation steps, in particular, no ultra centrifugation steps are required. This implies that short time centrifugation steps are necessary, which can immediately be derived from the wording of the particular passage (Henco column 4, line 47). Also, the wording

"more specifically no ultracentrifugation" suggests what kind of centrifugation is necessary; namely, a centrifugation step similar to ultracentrifugation, but one which does not require overnight centrifugating at 100 G or more.

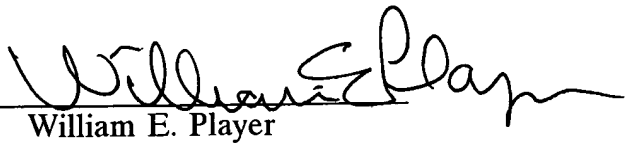
Centrifugation is necessary according to Henco since, if a sample is purified according to Henco having digested cells, such cell debris must be removed in order to have a proper working process. Therefore, centrifugation as taught in Henco would not have been suggested in combination with claim 61.

In any event, the issue is not whether present claim 61 excludes additional, unrecited process steps. The point is, Henco does not teach or suggest "a filter having decreasing pore size in the flow direction." The fact that Henco requires some form of centrifugation explains one reason why the "filter" recited in claim 61 would not have been an obvious modification of Henco based on the teachings of Hagen or Sternberg.

For the foregoing reasons, favorable action is requested.

Respectfully submitted,

JACOBSON, PRICE, HOLMAN & STERN, PLLC

By: 

William E. Player
Reg. No. 31,409

400 Seventh Street, N.W.
Washington, D.C. 20004-2201
(202) 638-6666
Atty. Docket: 10496/P58126NA
Date: September 5, 1996
WEP/tyb